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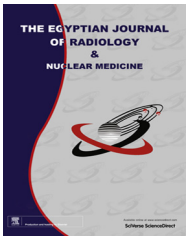

ORIGINAL ARTICLE

# Prognostic value of renal vascular impedance in patients with hepatic cirrhosis in risk for developing hepatorenal syndrome

**Ahmad Mohammad Ghandour** [a,*], **Ahmed Hamouda Ali Arnaout** [b]

[a] *Department of Radiology, Faculty of Medicine, Ain Shams University, Egypt*
[b] *Department of Internal Medicine, Faculty of Medicine, Zagazig University, Egypt*

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**KEYWORDS**

Renal Doppler;
Renal Vascular impedance;
Renal resistive index;
Renal pulsatility index;
Hepatic cirrhosis

**Abstract** *Aim of the work:* To evaluate the intrarenal arterial changes in patients with hepatic cirrhosis to anticipate development of hepatorenal syndrome.
*Materials and methods:* Study population included 155 subjects divided into five groups; group (1): control subjects; group (2): patients with compensated cirrhosis; group (3): patients with decompensated cirrhosis without ascites; group (4): patients with decompensated cirrhosis and ascites; and group (5): patients with hepatorenal syndrome.
*Results:* In group 5; the mean value of RI was significantly high as well as groups 4 and 3, as related to groups 2 and 1. The PI was significantly high in groups 5, 4, and 3, as related to groups 2 and 1. High RIs were received in 83% of group 5, 56% of group 4, 41% of group 3, 32% of group 2, and 8% of group 1. On the other hand, high PIs were received in 83% of group 5, 78% of group 4, 71% of group 3, 41% of group 2, and 3% of group 1. Renal vascular impedance measurement had sensitivity of 71%, specificity of 96%, PPV of 92%, and NPV of 86%.
*Conclusion:* Renovascular impedance values are good specific and positive predictive tools for hepatorenal syndrome development in patients with hepatic cirrhosis.


## 1. Introduction

Hepatic cirrhosis is defined histologically as a diffuse hepatic process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules. The progression of liver injury to cirrhosis may occur over weeks to years. Cirrhosis represents the final common histologic pathway for a wide variety of chronic liver diseases (1).

Cirrhosis of the liver is characterized by a profound disarrangement of the parenchyma and intrahepatic circulation,

* Corresponding author. Mobile: +971507725463.
E-mail address: ahmad_ghandour2003@yahoo.com (A.M. Ghandour).
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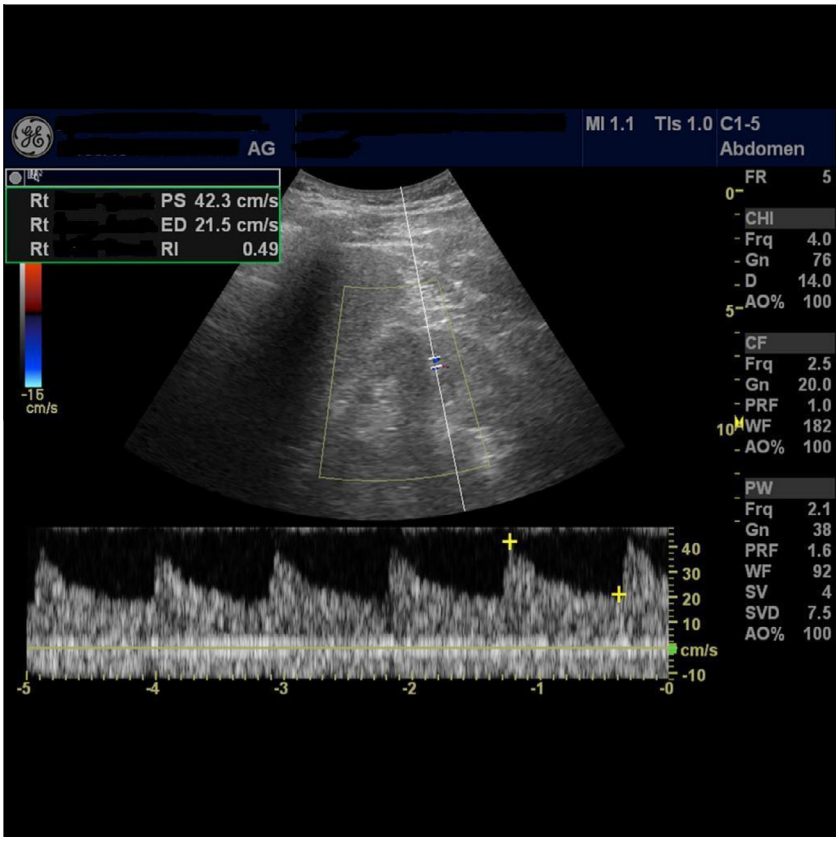


**Fig. 1** Triplex image for right renal interlobar artery showing normal RI.

which leads to portal hypertension. In later stages of the disease, the hemodynamic disturbances also involve the splanchnic and systemic circulatory beds (2,3).

Several vascular changes occur in the course of hepatic cirrhosis leading eventually into renal vascular changes with consequent renal function affection.

Hepatorenal syndrome (HRS) is the development of renal failure in patients with advanced chronic liver disease in the absence of any identifiable causes of renal pathology. Estimates indicate that at least 40% of patients with cirrhosis and ascites will develop HRS during the natural history of their disease (4,5).

The first detailed description of HRS was made by Hecker and Sherlock in 1956 (6). These authors reported 9 patients with cirrhosis or acute hepatitis who developed renal failure without associated proteinuria and with very low urinary sodium excretion. On autopsy, these kidneys showed normal histology. It was later shown that the kidneys from patients with HRS regain their function when transplanted into patients without cirrhosis, and that HRS can be reversible following liver transplantation (5).

The duplex Doppler waveform analysis of intrarenal arteriolar vessels provides a noninvasive estimate of renovascular impedance and renal arterial vasoconstriction; in particular, the renal resistive index (RI) and the pulsatility index (PI) which are reliable indicators of renal blood flow in patients with different pathologic conditions (7,8).

## 2. Aim of the work

The aim of this work is to evaluate the intrarenal arterial changes in patients with hepatic cirrhosis to anticipate development of hepatorenal syndrome.

## 3. Materials and methods

This prospective work was conducted starting October 2008 till January 2012.

The study population recruited in this work included 155 subjects (75 patients and 80 control subjects) divided into five groups as follows; group (1): 80 control subjects, 50 were males and 30 were females with mean age 40.5 years; group (2): patients with compensated cirrhosis included 22 patients, 16 were males and six were females with mean age 43.2 years; group (3): patients with decompensated cirrhosis without ascites included 17 patients, 12 were males and five were females with mean age 44.1 years; group (4): patients with decompensated cirrhosis and ascites included 18 patients, 14 were males and four were females with mean age 42.3 and group (5): patients with hepatorenal syndrome included 18 patients, 10 were males and eight were females with mean age 44.2 years.

Inclusion criteria were; (1) no hypertension, (2) no diabetes mellitus, (3) no previous renovascular disease, (4) no vascular disease that could affect the kidneys, (5) no renal abnormalities either congenital or acquired, (6) no transplanted kidneys, and

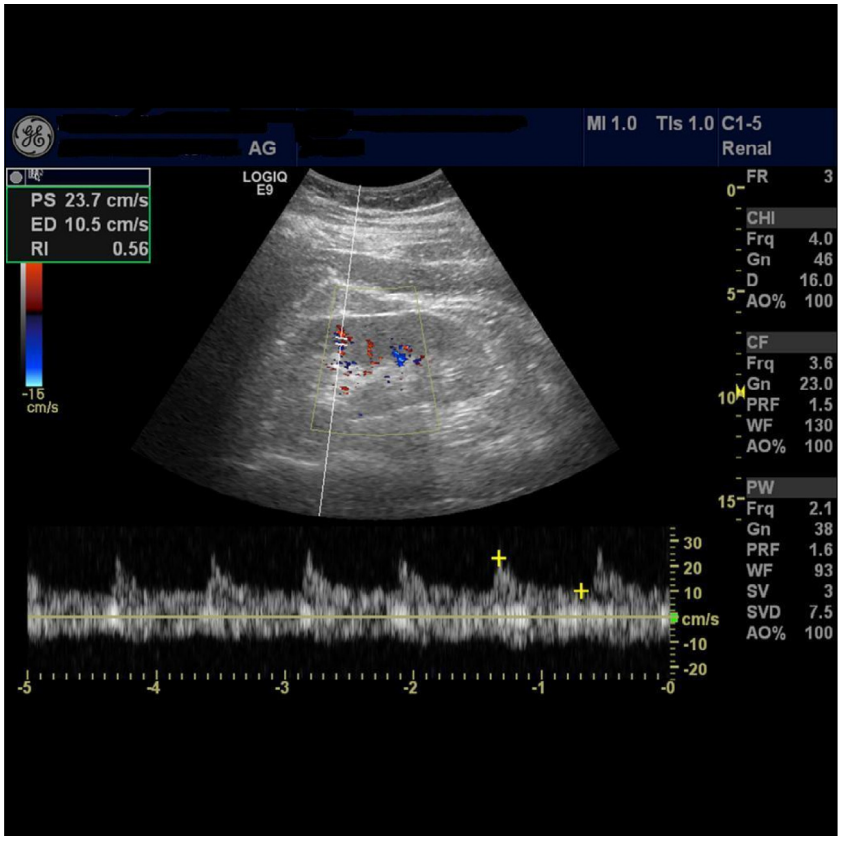


**Fig. 2** Triplex image for renal arcuate artery showing normal RI.

(7) subjects were considered control if they do not have any signs of chronic hepatic disease.

All patients were subject to clinical, sonographic, color Doppler, and laboratory assessment for the establishment of diagnosis and category.

Study was approved by the hospital ethics committee and a written informed consent was obtained from all patients.

### *3.1. Sonographic assessment*

After eight hours fasting, all of the patients and control subjects underwent abdominal ultrasonography (US) as a part of routine clinical evaluation by using US equipment with color Doppler capability using convex linear (frequency 2.8–5 MHz) transducer (Philips HDI 5000 SONOCT or GE Logic E9).

### *3.2. Color Doppler assessment*

The Doppler signal was recorded from both kidneys, from arcuate arteries at the level of the corticomedullary junction, or from interlobar arteries along the margin of the medullary pyramids. To minimize sampling error, the Doppler spectrum was increased by using the lowest frequency-shift range possible without aliasing and a low-frequency (100-MHz) wall filter. The RI and PI of three renal vessels, obtained in three renal areas (upper, middle, and lower poles), were measured in each patient by using at least three Doppler spectra, and the mean value was calculated. The RI and PI were automatically calculated on traces of 4–6 s by using the arterial Doppler US spectrum to avoid errors due to flow fluctuations. RI was calculated as $(S_{\text{peaksyst}} - S_{\text{mindias}})/S_{\text{peaksyst}}$, where $S_{\text{peaksyst}}$ is the peak systolic frequency shift and $S_{\text{mindias}}$ is the minimal diastolic frequency shift. PI is calculated as $(S_{\text{peaksyst}} - S_{\text{mindias}})/S_{\text{mean}}$, where $S_{\text{mean}}$ is the mean frequency shift. We considered normal values of renovascular impedance to be RI values lower than 0.70 (Figs. 1 and 2) and PI values lower than 1.20 (Fig. 3) (9).

### *3.3. Laboratory and clinical assessment*

Disease severity was assessed by using the Child-Pugh continuous score (10), which takes into account five conventional clinical (hepatic encephalopathy and ascites) and laboratory (albumin, prothrombin time, and bilirubin values) parameters (Table 1). Each variable is assigned a score of 1–3 according to the grade of abnormality. Thus, patients with compensated cirrhosis (class A) receive a total score of 5–6, those with slightly moderate decompensated cirrhosis (class B) receive a score of 7–9, and those with severely decompensated disease (class C) receive a score of 10–15.

## 4. Results

In group 5; the mean value of RI was significantly high (0.85) as well as groups 4 and 3 (0.80 and 0.74, respectively) (Figs. 4 and 5), as related to groups 2 and 1 (0.68 and 0.66, respectively).

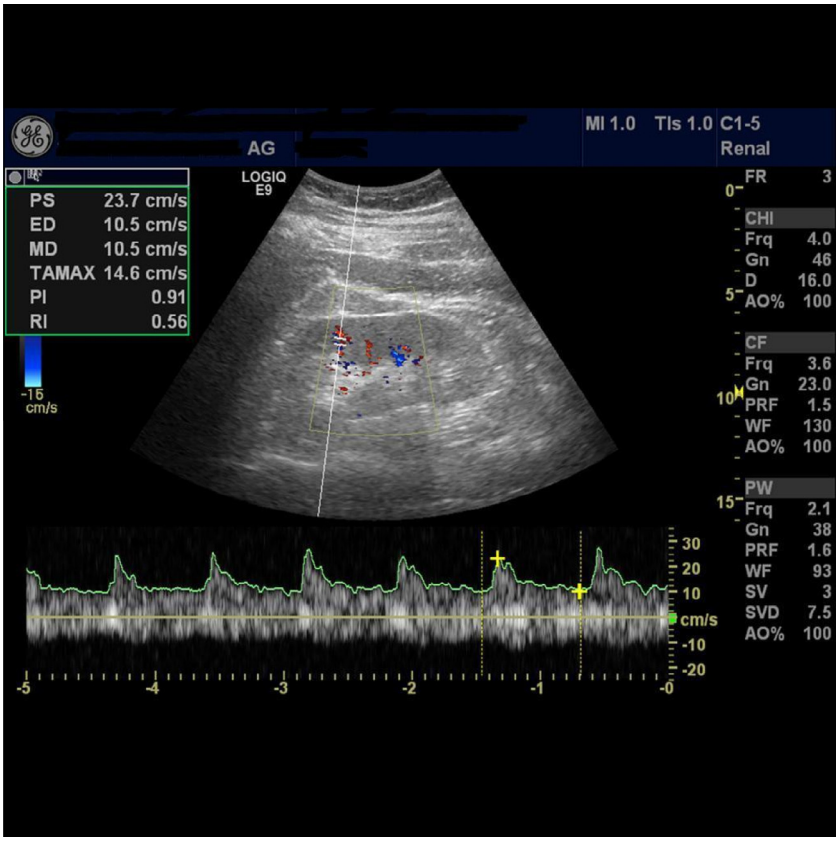


**Fig. 3** Triplex image for arcuate artery showing normal PI & RI.

**Table 1** Child-Turcotte-Pugh scoring system for cirrhosis (child class A = 5–6 points, child class B = 7–9 points, child class C = 10–15 points).

| Clinical variable | 1 Point | 2 Points | 3 Points |
|---|---|---|---|
| Encephalopathy | None | Stages 1–2 | Stages 3–4 |
| Ascites | Absent | Slight | Moderate |
| Bilirubin (mg/dL) | <2 | 2–3 | >3 |
| Albumin (g/dL) | >3.5 | 2.8–3.5 | <2.8 |
| Prothrombin time (seconds prolonged or INR) | <4 s or INR < 1.7 | 4–6 s or INR 1.7–2.3 | >6 s or INR > 2.3 |

The PI was also significantly high in group 5 (2.42) and groups 4 and 3 (2.21 and 1.63, respectively) (Fig. 6), as related to groups 2 and 1 (1.38 and 1.12, respectively).

High RIs were received in 83% of group 5 (15 out of 18 patients), 56% of group 4 (10 out of 18 patients), 41% of group 3 (seven out of 17 patients), 32% of group 2 (seven out of 22 patients), and 8% of group 1 (six out of 80 subjects).

On the other hand, high PIs were received in 83% of group 5 (15 out of 18 patients), 78% of group 4 (14 out of 18 patients), 71% of group 3 (12 out of 17 patients), 41% of group 2 (nine out of 22 patients), and 3% of group 1 (two out of 80 subjects).

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) are summarized in Table 2.

## 5. Discussion

In 1996, the International Ascites Club (6) published a consensus paper subdividing HRS into two types. Type 1 HRS is characterized by a rapid decline in renal function, defined as a doubling of serum creatinine to a level >2.5 mg/dL or a halving of the creatinine clearance to <20 mL/min within 2 weeks. The clinical presentation is that of acute renal failure. In type 2 HRS, renal function deteriorates more slowly, with serum creatinine increasing to >1.5 mg/dL or a creatinine clearance of <40 mL/min. The clinical presentation is that of stable renal failure in a patient with refractory ascites (6).

Renal failure in hepatorenal syndrome occurs because of vasoconstriction of the renal circulation and intense systemic arteriolar vasodilatation resulting in reduced systemic vascular resistance and arterial hypotension (5,11).

Duplex Doppler examination is a safe and reproducible technique for evaluating arterial blood flow, and it has been extensively validated as an indicator of renal vasoconstriction in various pathologic conditions, including obstructive or interstitial nephropathy, acute tubular necrosis, latent or full-blown hepatorenal syndrome (7,12–16), and cirrhosis with ascites (7,17,18). However, role of duplex Doppler examination in

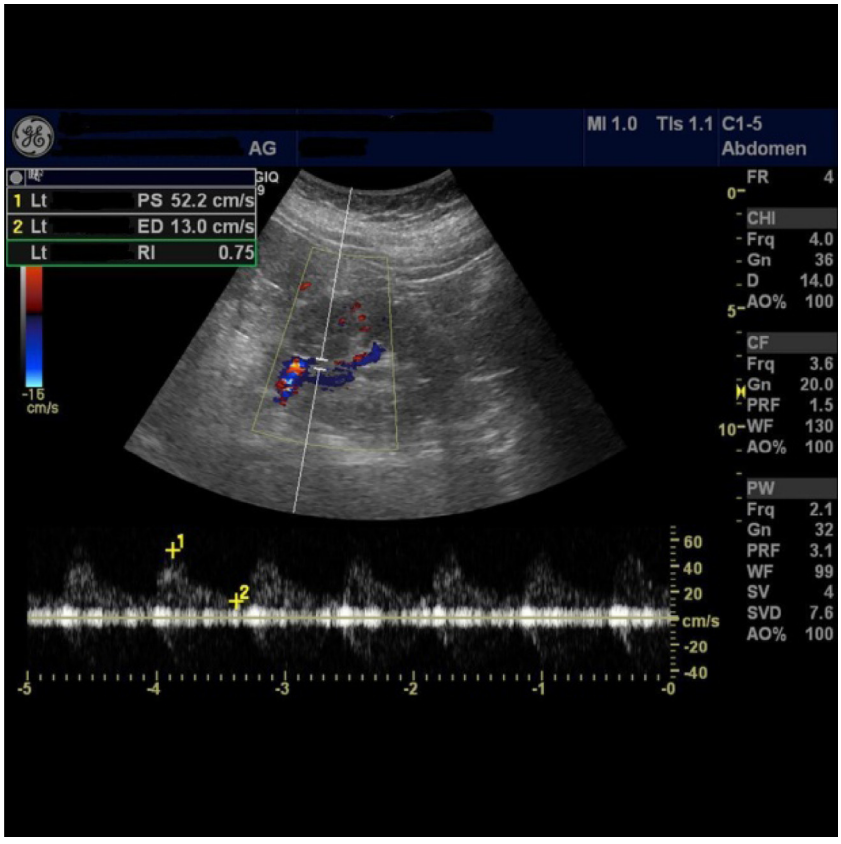


**Fig. 4** Triplex image for left renal interlobar artery in a decompensated cirrhosis patient with ascites showing high RI.

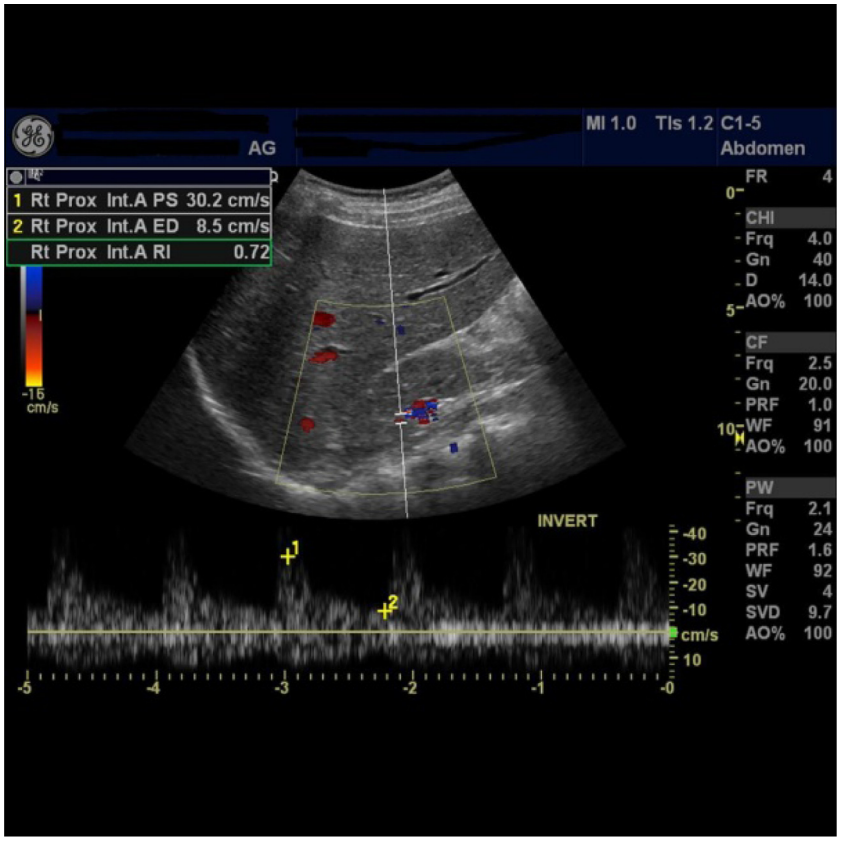


**Fig. 5** Triplex image for right renal interlobar artery in a patient with decompensated cirrhosis without ascites showing high RI.

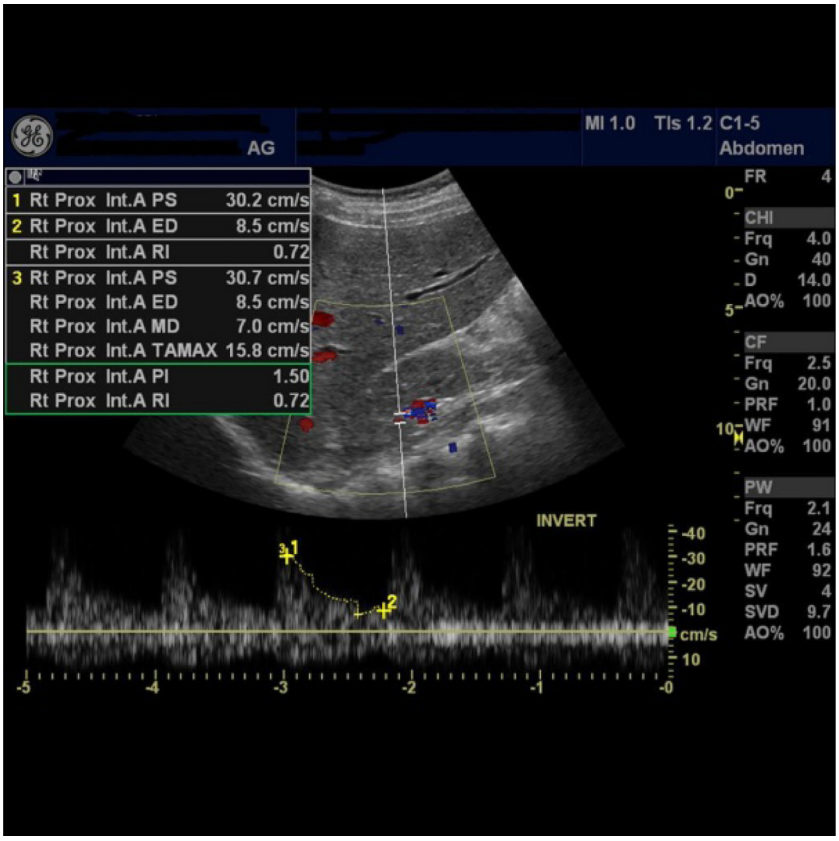


**Fig. 6** Triplex image for right renal interlobar artery in a patient with decompensated cirrhosis without ascites showing high RI & PI.

**Table 2** Sensitivity, specificity, PPV, and NPV.

| Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|
| 71% | 96% | 92% | 86% |

prediction of the development of HRS was not sufficiently evaluated by researchers.

Calculation of the renovascular impedance—expressed in terms of the resistance index and the pulsatility index—with use of Doppler tracings at the level of the interlobar arteries yields an estimation of renal arterial vasoconstriction (8,9,15).

Patients with cirrhosis have significantly higher renal RI and PI values compared with healthy subjects (8,9,13,19), and renovascular impedance increases as the liver disease progresses (9,20). These increases are marked in patients with ascitic cirrhosis (9,13). This is in accordance with our result of 56% of decompensated hepatic cirrhosis with ascites patients have high RI and 78% of the same group having high PI. In Annalisa et al. (9) work correlating renovascular impedance with portal pressure in patients with liver cirrhosis they found that; the RI and PI in the right renal artery (RRA) had a sensitivity of 52%, a specificity of 100%, a positive predictive value of 100%, and a negative predictive value of 33%. The RI in the left renal artery (LRA) had a sensitivity of 46%, a specificity of 86%, a positive predictive value of 92%, and a negative predictive value of 32%, while in the present work combining and averaging the RI and PI of right and left renal arteries gave comparative figures to the previous study – sensitivity of 71%, specificity of 96%, PPV of 92%, and an NPV of 86% – apart from the higher NPV in our study.

Colli et al. (21) found that in patients who have compensated (i.e., Child-Pugh class A) cirrhosis without ascites, high renovascular impedance correlates with the presence of esophageal varices. This is in accordance with our findings of higher impedance values in the group 2 than group 1 (RI 32%, PI 41% and RI 8%, PI 3%, respectively).

Agostino et al. (7) found elevated RI in 36% of their patients with Child-Pugh class A cirrhosis without ascites, which is related to 32% in the present study of same group of patients.

It has also been found that impedance values higher than the threshold for normal have prognostic value in the identification of patients who are at high risk for refractory ascites, hepatorenal syndrome, and death (9,13,22,23). Existing evidence therefore suggests that portal venous pressure is the initiating event that causes renal vasoconstriction (9).

The presence of renal dysfunction is often missed in patients with cirrhosis. Because of a reduction in muscle mass in these patients, serum creatinine may be within the normal range, even with a very low GFR. The use of blood urea nitrogen (BUN) concentration as a measure of renal function is even less reliable, because BUN levels can be affected by the presence of gastrointestinal bleeding or by the amount of protein in the diet (6), and here comes the major role of renal duplex Doppler assessment of renovascular impedance to pick

that sector of patients at high risk of developing renal failure and anticipating renal dysfunction.

## 6. Conclusion

From the present study we can conclude that renovascular impedance values (RI and PI) are good specific and positive predictive tools for hepatorenal syndrome development in patients with hepatic cirrhosis with consequent better early management and prognosis and also combining and averaging both renal artery impedance values give better negative predictivity than using either artery.

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